REMARKS

I. Formal Matters

The Examiner has rejected pending claims 23-28 and 31-39, and has withdrawn claims 40-50 from consideration as they are allegedly drawn to an invention that is independent or distinct from the invention originally claimed. The Examiner states that the withdrawn claims are directed toward invariant peptide sequences whereas the originally presented claims are directed toward peptidic variants.

Applicants believe this restriction is improper. While the Examiner has alleged that the claims are drawn to independent and distinct inventions, he has not shown that it would be a burden to examine the claims together. The law requires that both (1) the inventions are independent and distinct, and (2) there would be a serious burden on the Examiner if restriction was not required. M.P.E.P. § 803. The Examiner has focused on only the first part of this two-part test. In order to properly restrict the groups, the Examiner needs to show that there would be a serious burden in examining the claims together.

Applicants believe that there would not be a serious burden in Examining the groups together. Specifically, claim 40 is directed to particular embodiments within independent claim 23, and thus falls within that genus claim. Claims 41-50 are directed to methods of using very similar peptides, as well. Applicants believe it would not be a burden to examine all the claims together. Thus, Applicants request that the restriction requirement be withdrawn.

II. Written Description Rejection

The Examiner has rejected claims 23-28 and 31-39 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. The Examiner argues that the original application does not provide adequate support for the broadly claimed genus of immunogenic polypeptide fragments comprising HIV-1_{MAL} epitopes of 5-150 amino acid residues, wherein at least one amino acid residue is substituted at one of the specific positions.

The Examiner provides three reasons for his conclusion. First, he argues that the disclosure fails to identify any specific HIV-1_{MAL} immunogenic fragments of the claimed lengths and substitutions. Second, the Examiner argues that the disclosure fails to perform any type of comparison, wherein specific immunogenic fragments from isolate MAL are identified and acceptable amino acid substitutions are performed. Third, the Examiner alleges that the disclosure fails to provide adequate support for MAL-specific polypeptides of the recited lengths. The Examiner disagrees with Applicants' argument that figures 3E-F provide support for the claimed invention.

Applicants have previously presented arguments against this rejection and now enclose the Declaration of Dr. Marie-Lise Gougeon in support of these arguments.

Applicants had amended the claims in the last response because the Examiner was concerned about whether the claims provided information on which amino acids were mutated and what peptide lengths were supported in the application. With respect to the peptide length, Applicants point to the statement in the specification that peptides comprising or **consisting of** the conserved regions (which have the lengths of 21, 43,

79, 94, and 131, respectively) are included in the invention. *See* page 23. This very specific disclosure provides support for peptides having the claimed lengths. Applicants maintain that it is not necessary to recite the length (for example 21 amino acids) when a peptide with that length is disclosed in the specification (for example 680-700). The same concept is conveyed, irrespective of how it is described. *See* Declaration of Dr. Gougeon, ¶ 6.

With respect to the location of the mutations, Applicants maintain their positions that the identity of the mutations encompassed by the invention could be ascertained by considering Figure 3. Applicants believe that comparison of the various Env sequences in Figure 3 highlights positions where an amino acid is substituted in all of the sequences designated LAV_{MAL}, ARV2, and LAV_{ELI} when compared to LAV_{BRU}. This shows that this particular amino acid is not required for immunogenicity. *See* Declaration of Dr. Gougeon, ¶ 7-8. This information assists one in understanding which Env sequences were not required for immunogenicity and shows that this was understood by the inventors at the earliest filing date, as mentioned in the specification on page 16, line 30 through page 17, line 14. The claims include a listing of these nonconserved amino acids, which are targets for mutation. *See* Declaration of Dr. Gougeon, ¶ 8. The specification states on page 23 that "[p]roteins containing or consisting of the 'well conserved stretches' are of particular interest." This was well known in the art at the time of filing of this application for other antigenic systems. Several recent studies also support this statement, both at the cellular (Frahm et al., J. Virol 78:2187 (2004)) and humoral (Yang et al., J. Virol. 78:4029 (2004)) level, and the

use of consensus sequences in vaccine design to minimize the genetic differences between vaccine strains and contemporary isolates is currently being considered (Gaschen et al., Science 296:2354, 2355, second paragraph (2004); and Gallo, Lancet, early online publication, last paragraph of p.3 (September 28, 2005); Burton et al., Nature Immunol. 5:233-236, 235 'strategies for immunogen design' paragraph (2004))

Applicants added claim 40 in the prior response to recite that the peptides comprise certain conserved sequences. The conserved sequences are recited on page 23, and the text following the sequences recites that "[p]roteins containing or consisting of the 'well conserved stretches' are of particular interest." Therefore, Applicants believe peptides comprising these conserved regions are adequately supported in the specification.

Furthermore, reference to the conserved sequences, such as those recited on page 23 of the specification, provides a substantial link between the structure of the claimed peptide and its recited function as conserved sequences are well recognized for maintaining a protein's function. *See* specification page 12, lines 11 to 14, stating that the inventors already knew that well-conserved stretches are "associated with important biological function." Additionally, *see* specification page 16, lines 8 to 16, stating that the inventors had already identified the immunogenic capacity of the peptides consisting of or comprising the well conserved stretches of the Env protein of HIV-1. *See* Declaration of Dr. Gougeon, ¶ 10-13.

The specification suggested in 1986 that conserved regions of HIV proteins contribute to the induction of neutralizing antibodies to those proteins. This has been

confirmed. *See* Holmbach et al., J. of Virology 67:1612-1619, 1617, second column, first and last paragraph (1993); Spenlehauer et al., J. of Virology 72:9855-9864, 9862, last paragraph of the first column (1998). *See id* ¶ 13.

Therefore, Applicants request that the Examiner withdraw this rejection.

III. Conclusion

Applicants request that the Examiner reconsider the pending claims, especially in light of the Declaration of Dr. Gougeon.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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